
The Story of Vaccines

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Animals

The Smallpox Vaccine

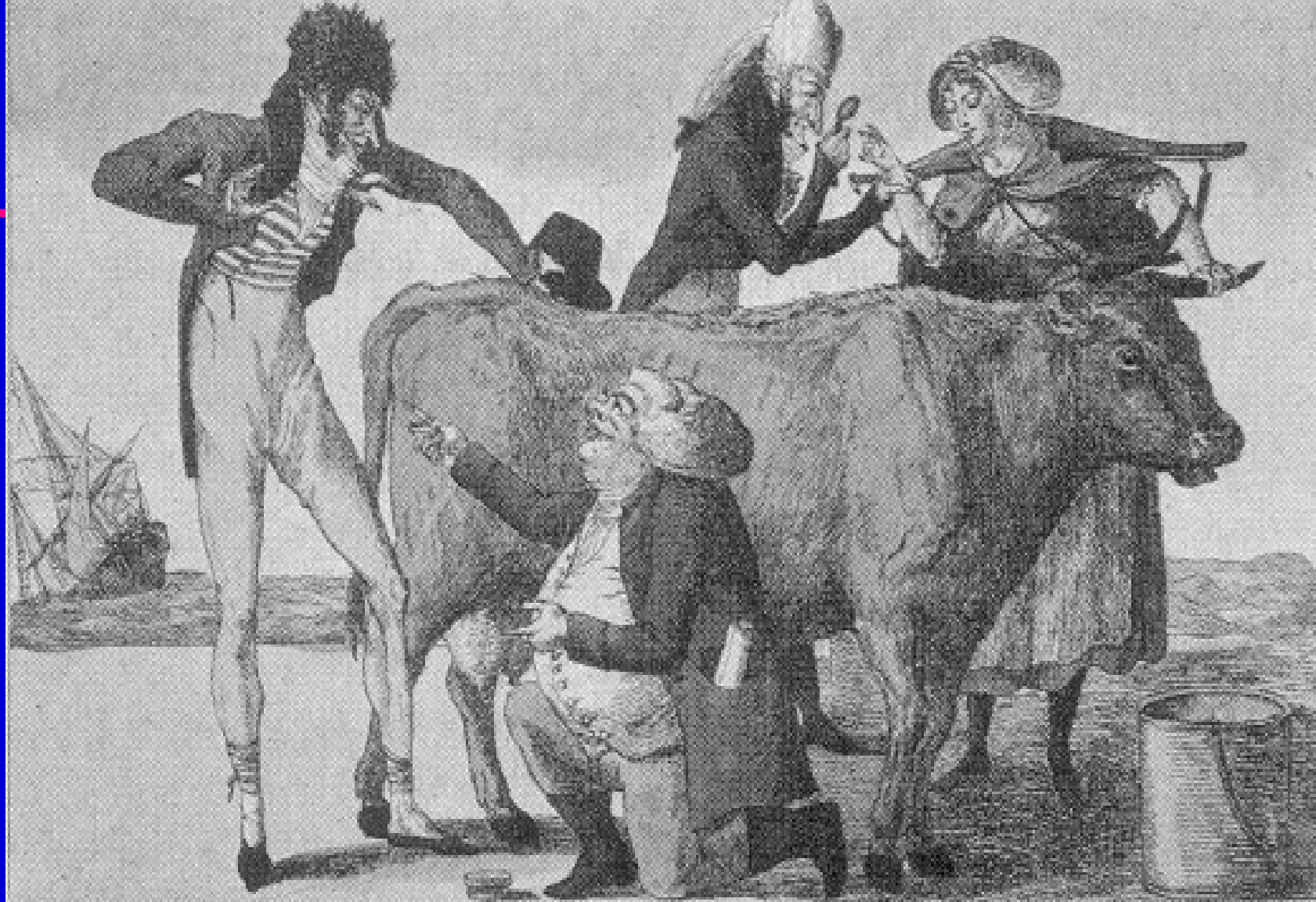
(late 1700s)



Smallpox

Smallpox Vaccine: Method of Attenuation

- **Jenner used cowpox, a heterologous host (non-human) virus**
- **Cowpox was less capable of inducing disease than human smallpox but was antigenically similar**
- **Goal of all vaccines is to separate**



L'ORIGINE DE LA VACCINE.

A Paris chez Depaille, Rue des Mathurins, la Banque aux deux Plâtres d'Or.

Deposé et de l'

A



Smallpox

- **Estimated to have killed about 500 million people**
- **Disease has been eliminated by worldwide vaccination. Last case of natural smallpox occurred in Ethiopia in 1977**

The Rabies Vaccine

(late 1800s)

Rabies Vaccine: Method of Attenuation

- **Pasteur grew rabies virus in rabbit spinal cords. Spinal cords were then dried for days or weeks**
- **Attenuation was by partial killing**
- **But use of spinal cords (which contain myelin**



M. Pasteur.
AN INOCULATION FOR HYDROPHOBIA.—FROM "L'ILLUSTRATION."

The Polio Vaccine

(1930s)

Tissue Culture

Tissue Culture

- **Hugh and Mary Maitland, working in Manchester, England, grow vaccinia virus in chopped up chicken kidneys**
- **Growing viruses in laboratory cells easier than growing viruses**

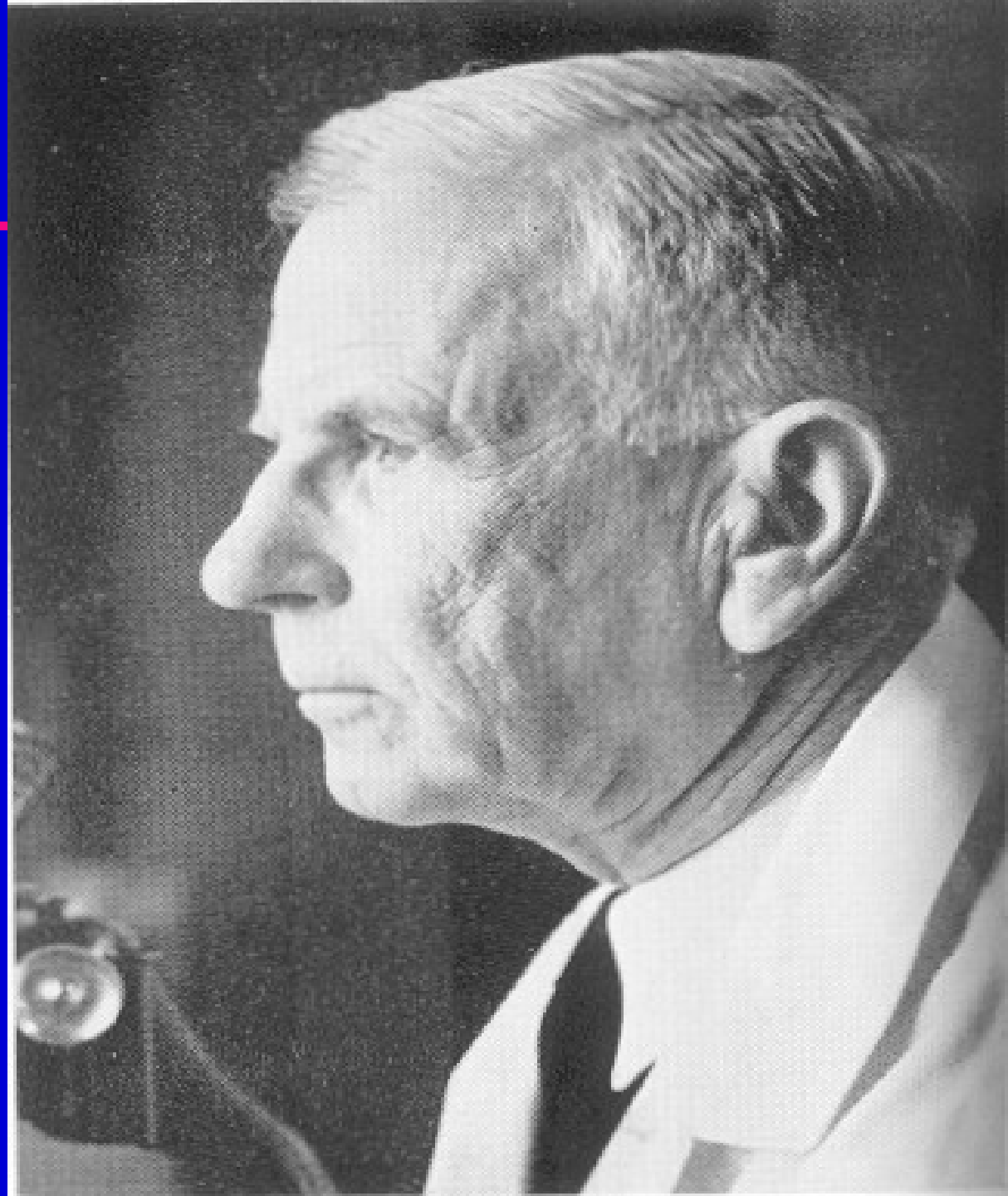
The Yellow Fever Vaccine (1930s)



Concept of Viral Attenuation

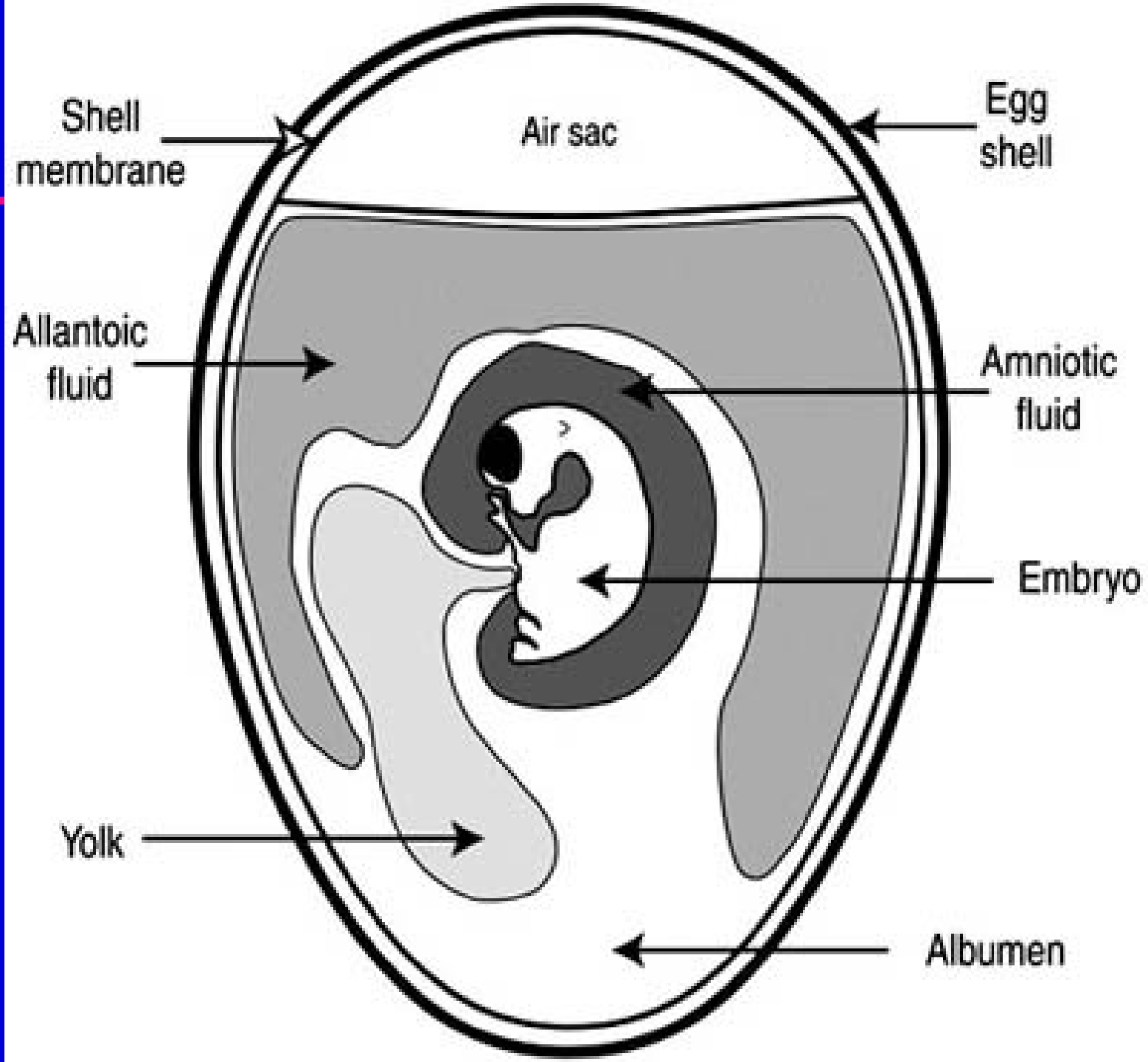
- Using the Maitlands' technique, Max Theiler took yellow fever virus and serially passaged it in minced preparations of mouse brains, mouse embryos, and chick embryos
- Theiler reasoned that serial passage in non-human cells would attenuate viral growth in

Eggs



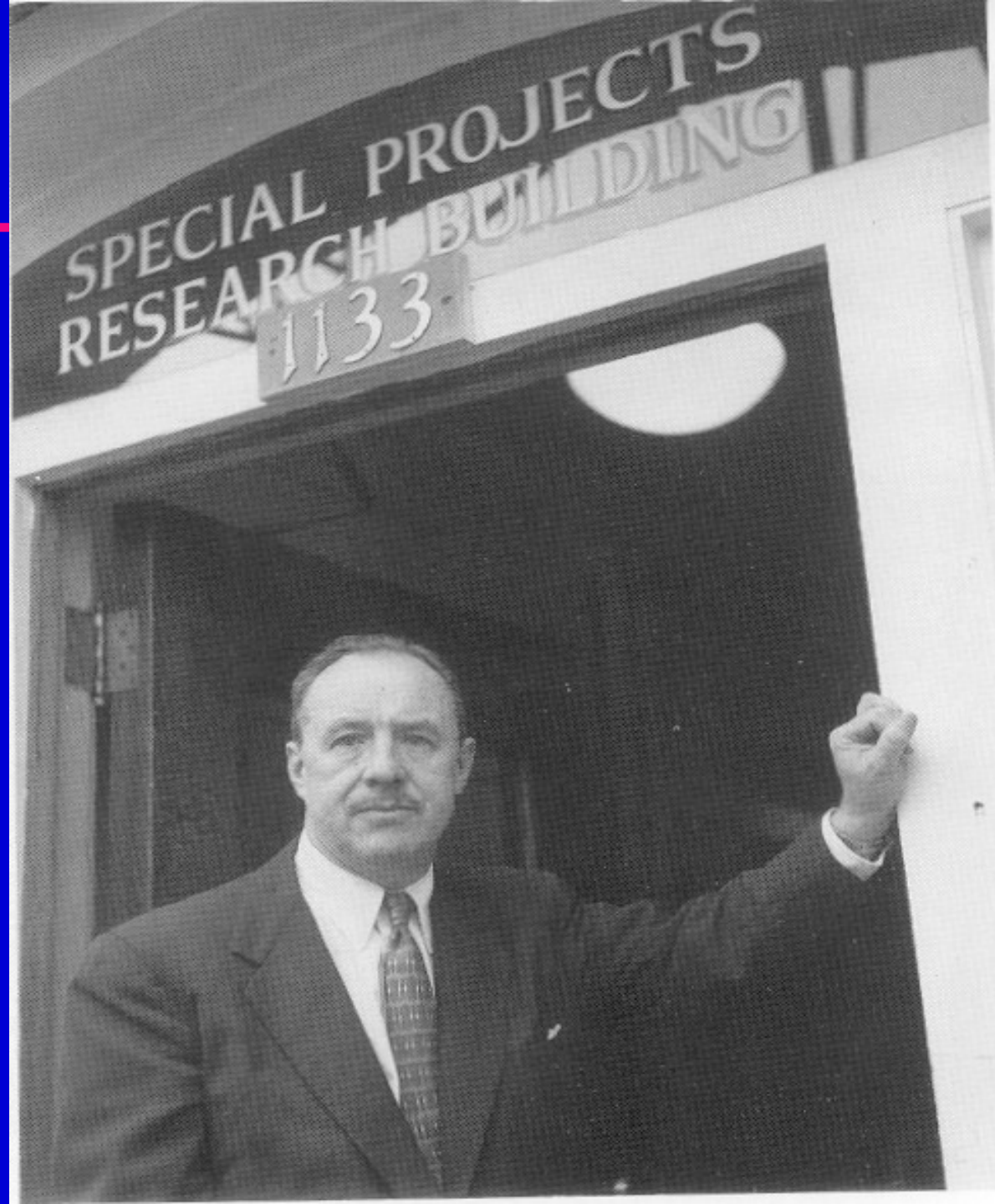
Eggs

- Ernest Goodpasture found that viruses could be propagated in the chorioallantoic membrane that surrounded the chick embryo. Showed that at least 30 viruses grew in eggs



The Influenza Vaccine

(1940s)



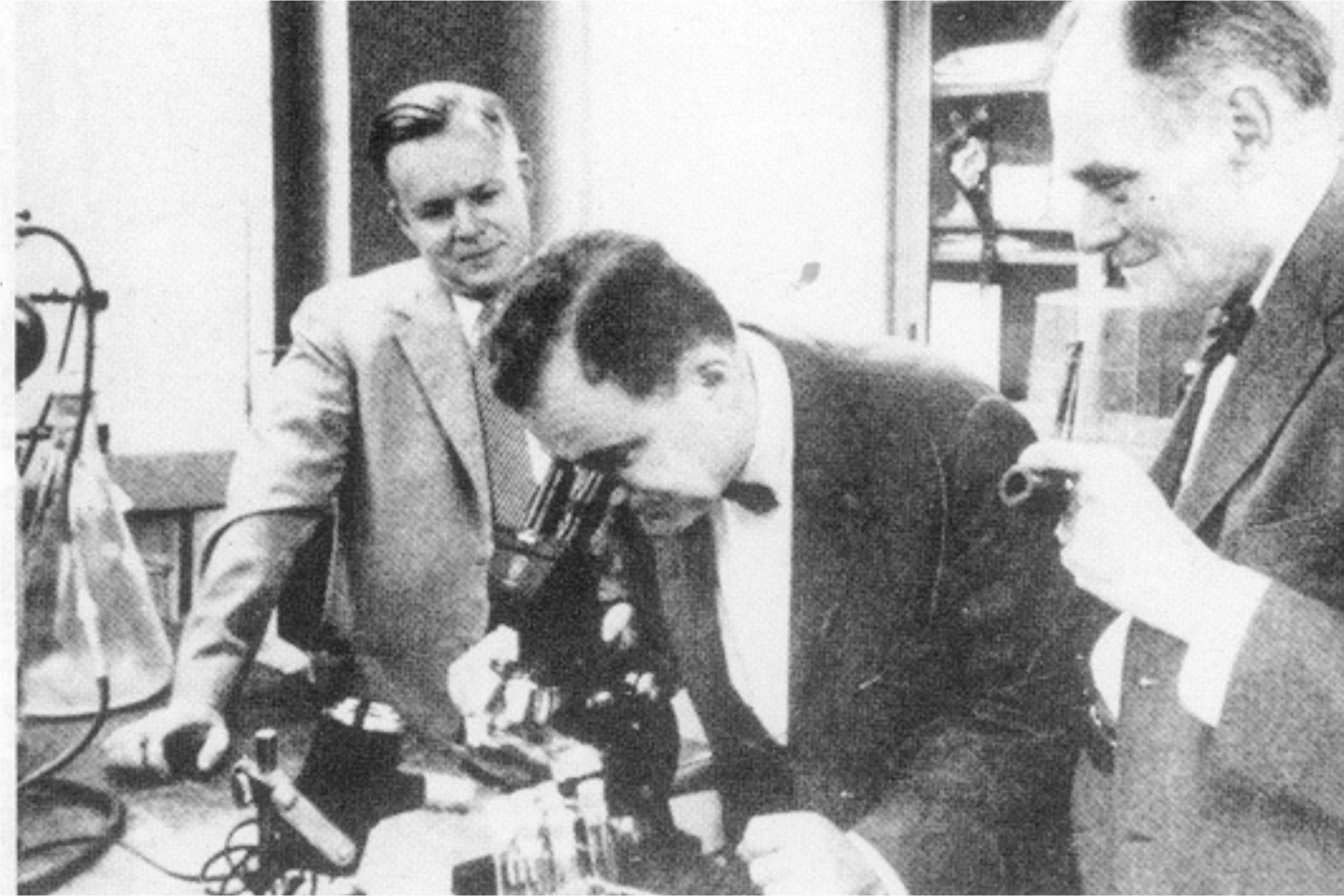
Influenza Vaccine

- Francis propagated influenza viruses in eggs, harvested the allantoic fluid, and killed influenza virus with formaldehyde

Cell Culture

The Polio Vaccine

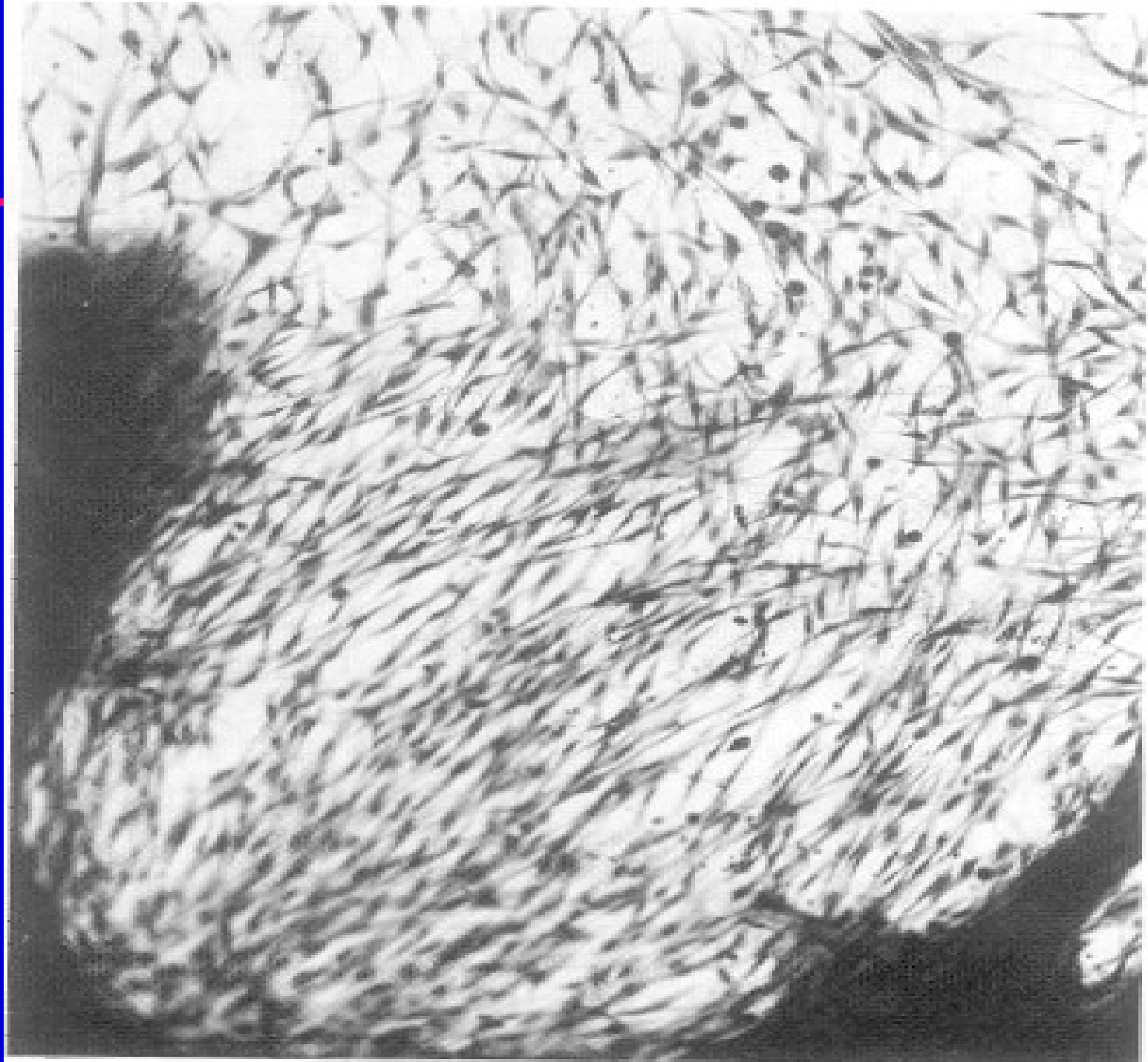
(1950s)



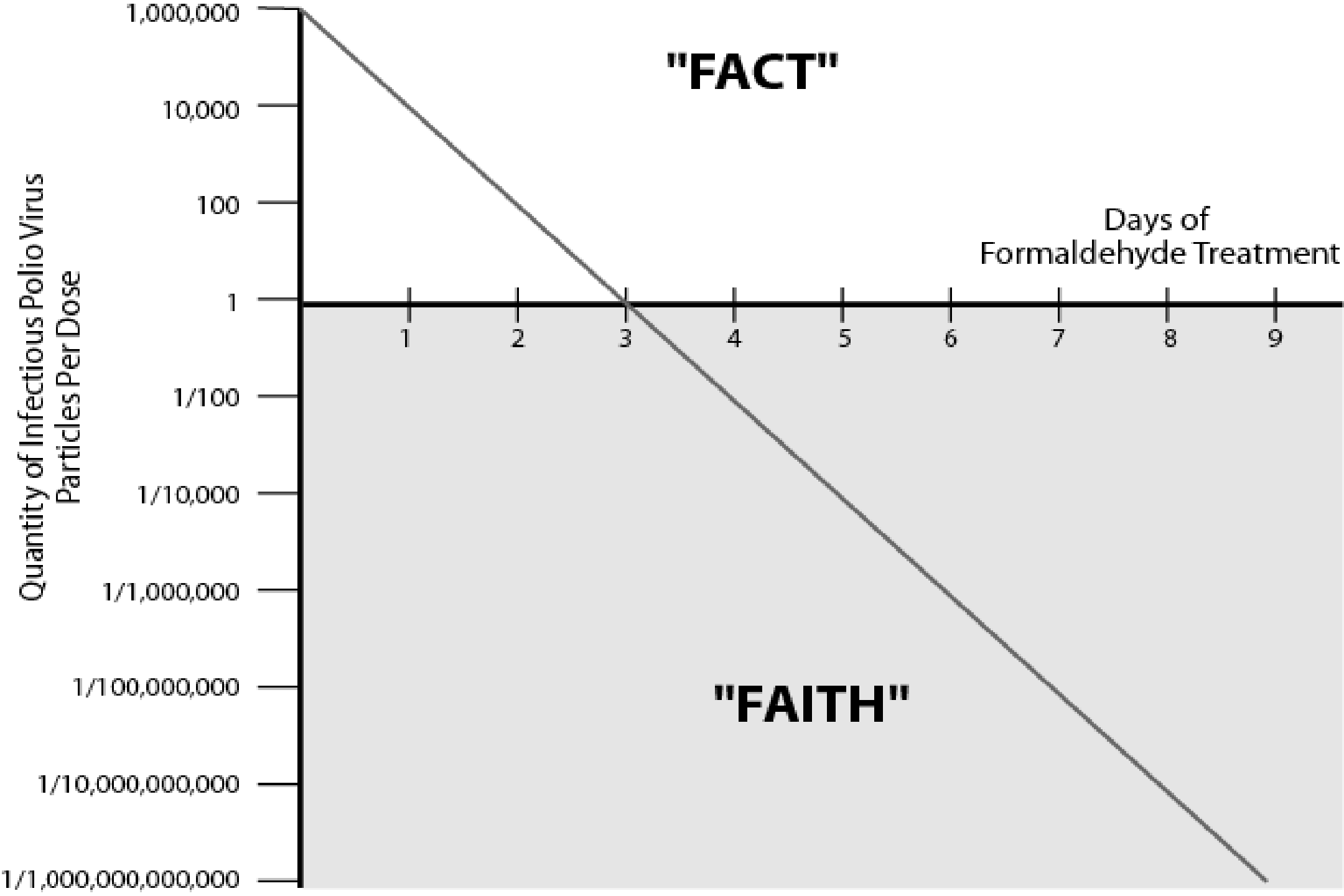
Enders, Weller, and Robbins

- Adapted polio virus to growth in cell culture
- Allowed polio virus to be grown in large quantities
- Obviated the need for monkey spinal cords as a source of virus. Nobel Prize in 1954











The Salk Vaccine

- **Three doses of vaccine given to 420,000 children**
- **200,000 children inoculated with placebo and 1.2 million observed, uninoculated**
- **Efficacy was 65% against type 1, 100% against type 2, and 96% against type 3 induced polio**



Polio in the United States: 1955-1962

Number of cases of paralysis

1955	29,000
1956	15,000
1957	5,500
1958	5,500
1960	3,200
1961	1,300
1962	900



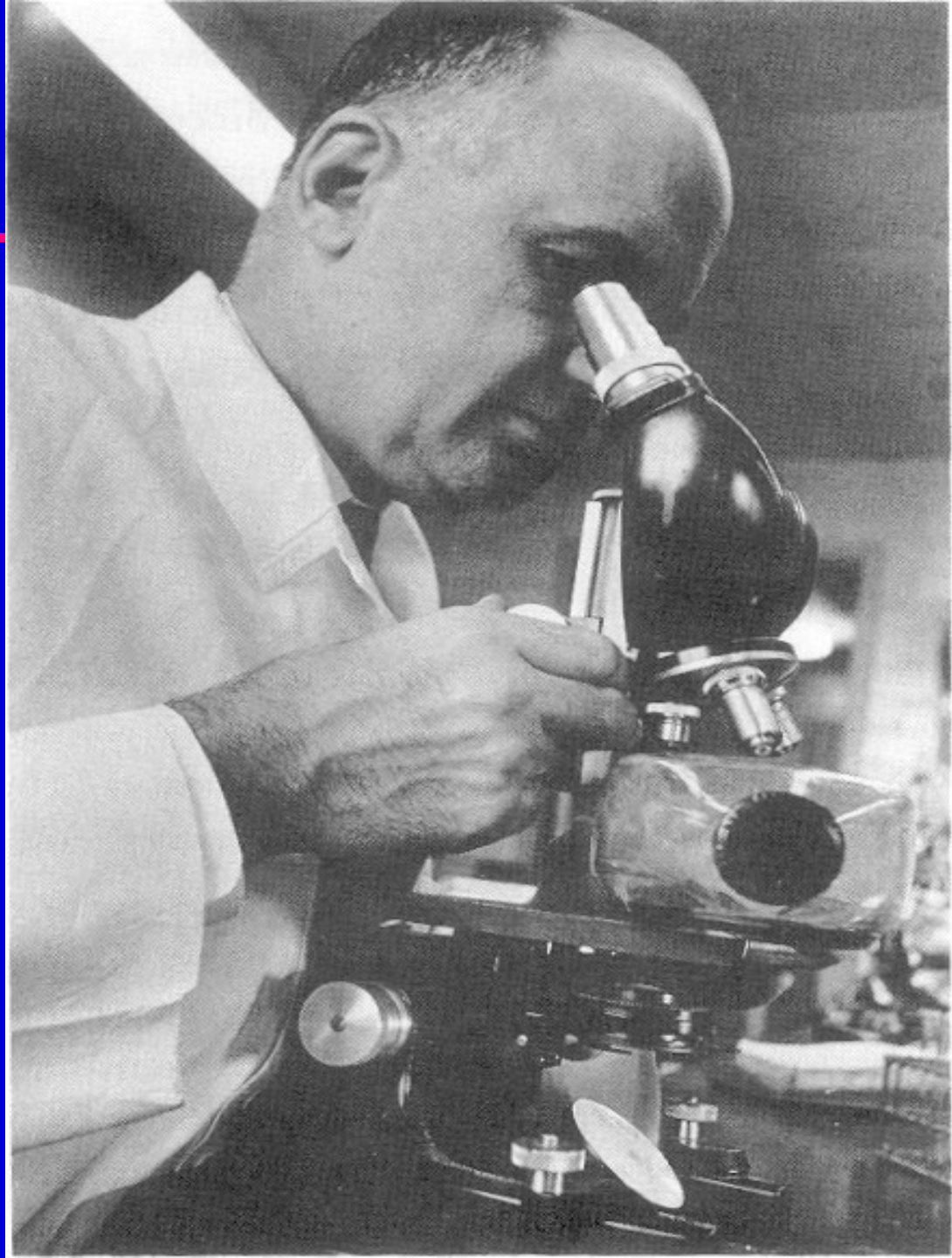
The Sabin Vaccine

- Using Theiler's technique of viral attenuation in non-human cells, and Enders' technique of cell culture, Sabin attenuated types 1, 2, and 3 polio viruses in monkey kidneys and monkey testicular cells



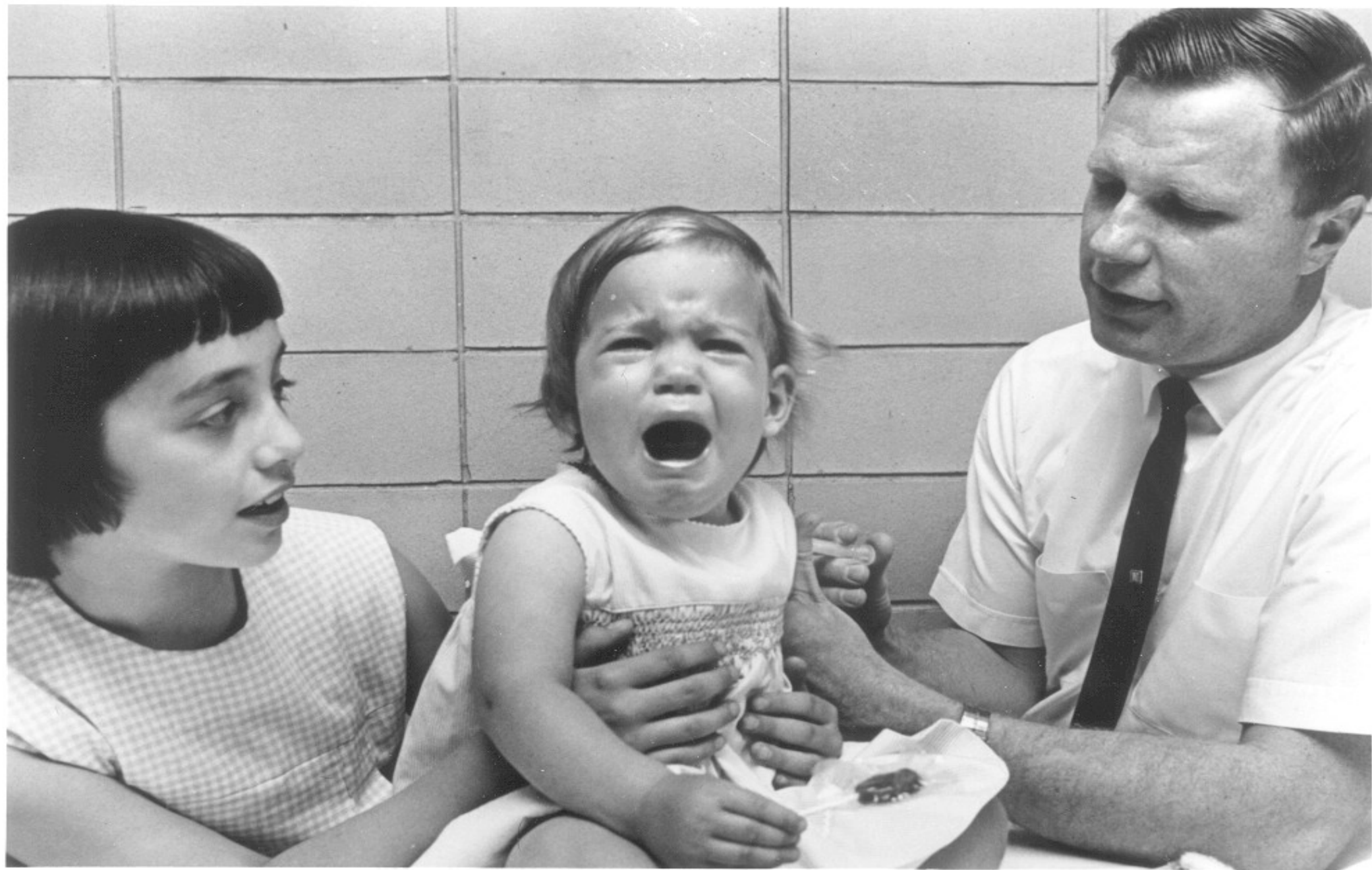
The Mumps Vaccine

(1967)

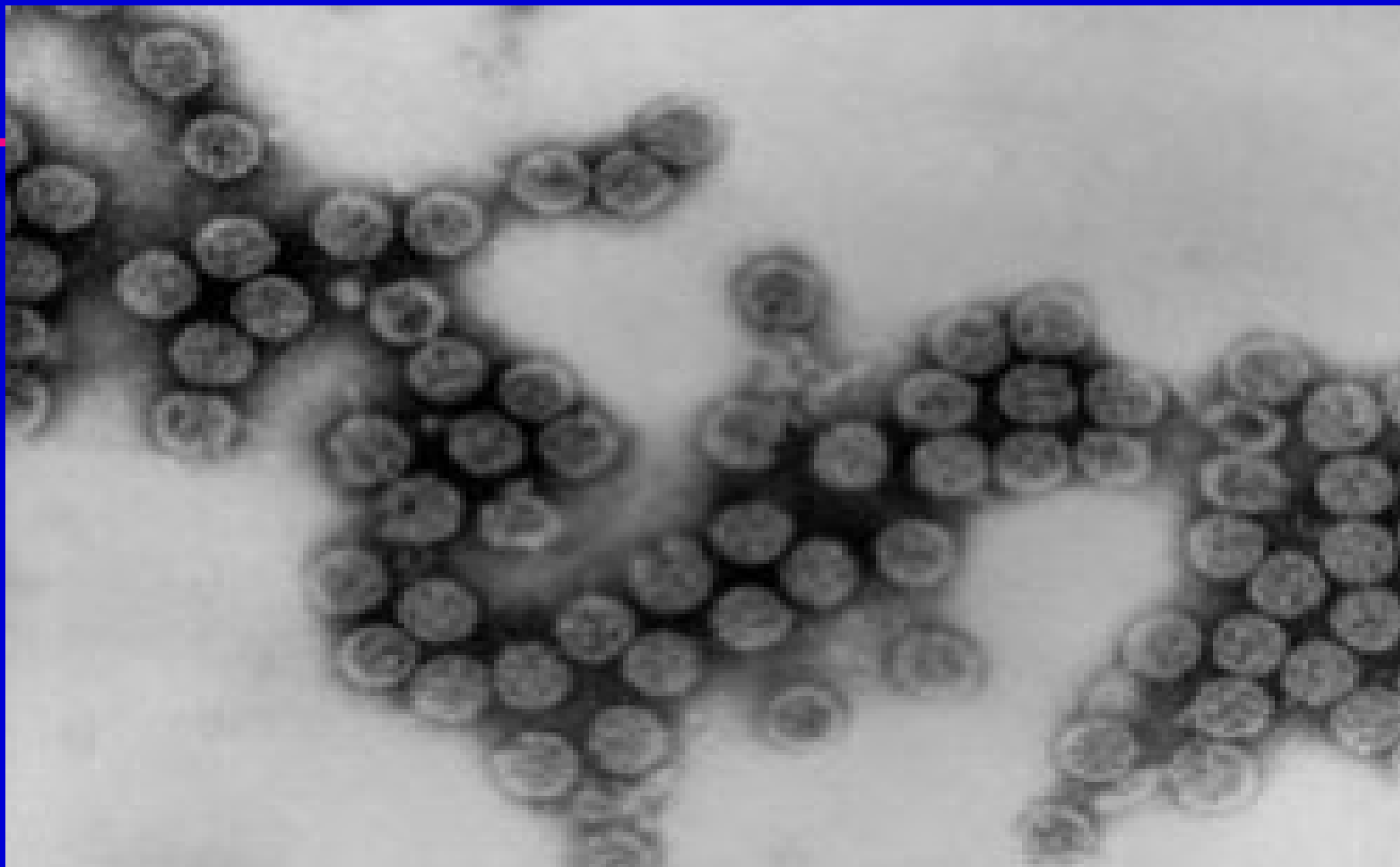


The Mumps Vaccine

- **Maurice Hilleman isolated mumps from his daughter, Jeryl Lynn**
- **Jeryl Lynn strain attenuated by serial passage in chick eggs and chick embryo fibroblast cells**



Human Fetal Cells



SV40



Vaccines made in human embryo cells

- **Hepatitis A**
- **Varicella**
- **Rubella**
- **Rabies**

Blood

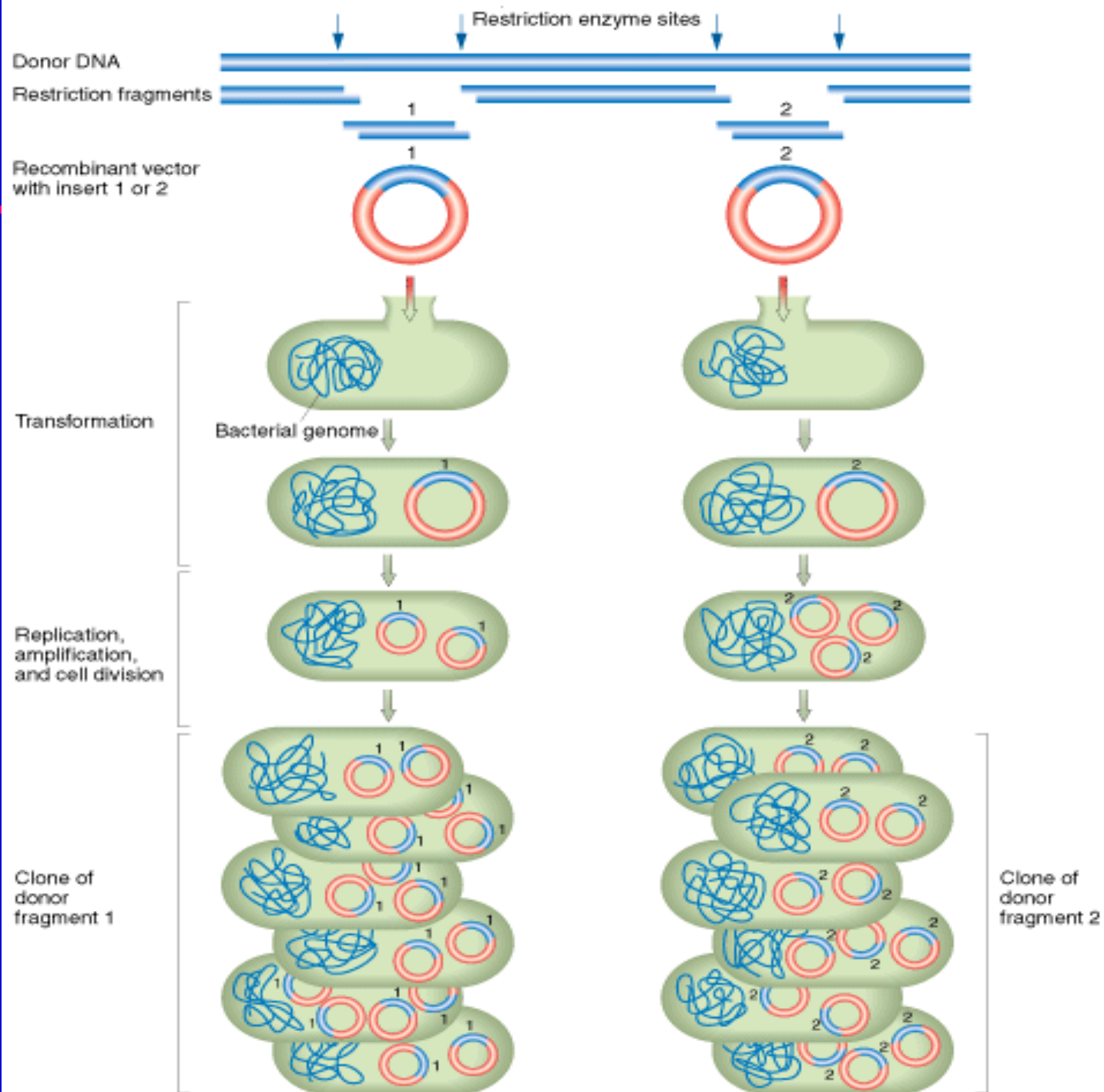
The Hepatitis B Vaccine

The First Hepatitis B

Vaccine

- **Maurice Hilleman took plasma from people infected with hepatitis B virus (contains whole live virus and HBsAg) and treated preparation with pepsin, urea, and formaldehyde**

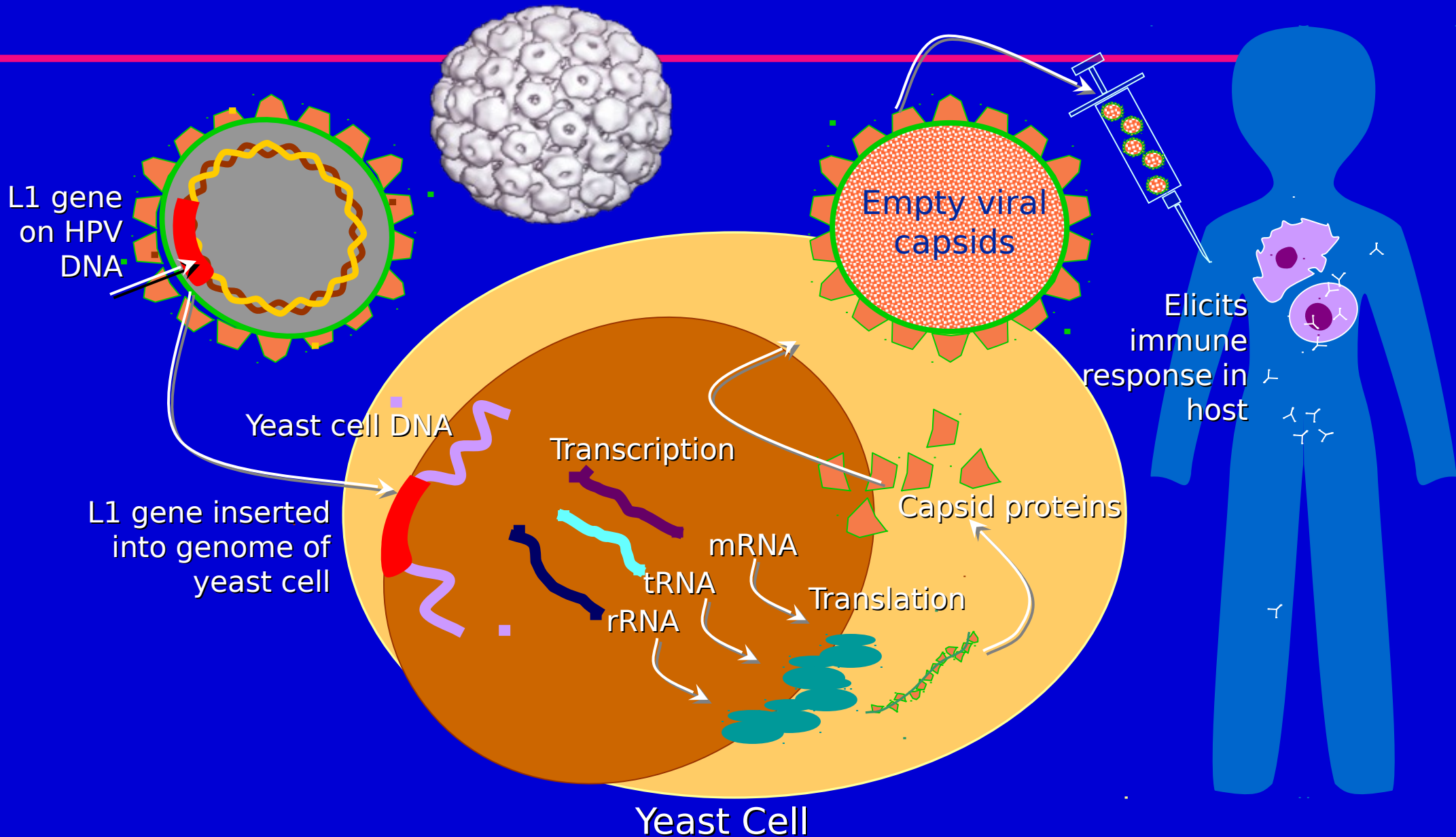
Recombinant DNA



The Second Hepatitis B Vaccine

- **Hilleman's hepatitis B vaccine was the first to use recombinant DNA technology and the first to prevent a cause of cancer**

HPV L1 VLP Vaccine Synthesis



The Birth of Fear

The Pertussis Vaccine (1982)

DPT: Vaccine Roulette

- **Anti-vaccine movement in America born on April 19, 1982**
- **Lea Thompson and “DPT: Vaccine Roulette”**
- **Showed series of children with permanent brain damage following DTP vaccine**

The pertussis vaccine

- **Media coverage claiming that the whole-cell pertussis vaccine caused brain damage**
- **Flood of lawsuits successfully claiming that pertussis vaccine caused SIDS, Reye's Syndrome, coma, mental retardation, epilepsy, and transverse myelitis**

Pertussis science matures, but too late

- **Epidemiological studies during next 10 years showed no increased risk for epilepsy, retardation following pertussis vaccine**

Impact of lawsuits

- **Price of DTP vaccine rose from \$0.19 in 1980 to \$12.00 in 1986**
- **Number of OPV vaccine makers declined from 3 to 1, of measles vaccine from 6 to 1, and of pertussis vaccine from 8 to 1.**
Birth of NCVIA and the VICP

NVIC

- **Continues to weigh in on vaccine safety**
- **Notion that vaccines have merely replaced infectious diseases with chronic diseases**
- **NVIC is media savvy, politically connected, and lawyer-backed**

Introduction of new vaccines

- Hib: diabetes
- Pneumococcus: seizures
- HBV (adolescents) MS
- HBV (newborns) SIDS
- HPV blood clots, strokes, CFS





Novel H1N1 Vaccine, 2009

- **Contains harmful preservative: thimerosal**
- **Contains harmful adjuvant: squalene**
- **Not adequately tested**
- **CNN: Which Is Worse: Vaccine or Virus?**

Other Fears

- **Anthrax vaccine**
- **Eric Delwart and deep sequencing**
 - Porcine circoviruses

Consequences of Fear

Current outbreaks

- **Pertussis, Delaware 2006**
- **Measles epidemic, 2008**
- **Hib deaths, 2009**

The Voice of Society

- Hospitals mandating influenza vaccine
- Doctors choosing not to see unvaccinated patients in their practice
- Parents concerned about sending children to day-care centers, classrooms (Tatel, Yarkin, Flint)